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| EXAMINER | |
|---|---|
| MERTZ, PREMA MARIA | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/510,413 | AUER ET AL. | |
| | Examiner | Art Unit | |
| | Prema M. Mertz | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *6-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/6/04, 5/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

***Election/Restrictions***

1. Applicant's election without traverse of Group I (claims 1-5) in the reply filed on 8/16/07 is acknowledged.

Claims 6-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

***Claim Rejections - 35 USC § 112, first paragraph***

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2a. Claims 1-5, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying an inhibitor of complex formation of an ARE-containing mRNA and an HuR protein by providing a soluble HuR protein wherein the soluble HuR protein is selected from the group of proteins consisting of the amino acid sequences set forth in SEQ ID NO: 3 and 4, as set forth in claim 1, does not reasonably provide enablement for a method as recited in claim 1 in which HuR is a soluble form of a recombinant full-length protein or a variant or mutant of a soluble form of a full-length protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are drawn very broadly to a method for identifying an agent that has an inhibitory effect on complex formation of ARE-containing mRNA with all soluble HuR proteins.

However, other than inhibiting complex formation of an ARE-containing mRNA and a soluble form of HuR protein selected from the proteins consisting of the amino acid sequences set forth in SEQ ID NO:3 and 4 (see specification, page 4, lines 26-33; Example 5, pages 18-20), the specification fails to provide any guidance for the successful use of any other HuR proteins or variants or mutants thereof.

The specification delimits the instant HuR protein by reference to a specific amino acid array as set forth in SEQ ID NO:1 or 2 (see page 5, lines 1-4), however, in claim 1, the protein is defined by reference to the abbreviation HuR, wherein the abbreviation itself does not represent any distinguishing information concerning the disclosed protein. Moreover because HuR does not inherently correspond to any particular protein, claims that lack the recitation of structural properties encompass subject matter not supported by the instant specification. Molecules that are embraced by the claims are not adequately supported by the instant specification because the specification provides no guidance for how to make such molecules nor are examples provided as to how these molecules would be identified commensurate with the breadth of the claims. In the absence of an appropriate structural and/or functional reference, a person of ordinary skill in the art would be unable to make and use the molecules embraced by the claims without undue experimentation because one could not distinguish the proteins envisaged by the specification and those, which are unrelated.

The specification delimits the instant method to contacting a soluble HuR protein consisting of the amino acid sequence set forth in SEQ ID NO:3 or 4 with an ARE from IL-2, IL-4, IL-8, Cox-2, IL-1β or TNF-α (see Example 5, page 18, lines 20-27). However, with respect to claim 1, as recited, what is claimed in the instant invention broadly encompasses a method of

identifying an inhibitor of complex formation using all HuR proteins including variants and mutants thereof. The specification is non-enabling for a method of using these unlimited and unidentified number of substances, which are encompassed by the scope of the claims. Claim 1, for example, is a single means claim (M.P.E.P. 2164.08(a)). In In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), the Courts have held that: A single means claim, i.e. where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor). Since no material limitations for "HuR protein" have been recited in the claim and only a biological activity has been recited, the claim encompasses every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to Hyatt. The claimed invention encompasses a method of using compositions not envisioned or described in the specification, and neither does the specification disclose how these compositions can be distinguished from each other. The specification only enables a method of using a HuR protein as set forth in SEQ ID NO:3 or 4. The properties of this protein may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other proteins are encompassed by the scope of the claims is practically infinite and the guidance

provided in the specification very little, thereby rendering the results of the methods taught in the specification unpredictable (see pages 18-20). Therefore, it would require undue experimentation to determine which other proteins would be encompassed by the scope of the method claims. The disclosure of using a soluble HuR protein of consisting of the amino acid sequence set forth in SEQ ID NO:3 or 4 wherein said protein forms a complex with ARE-containing mRNA, is clearly insufficient support under the first paragraph of 35 U.S.C. 112 for claims, which encompass a method of administering every and all HuR proteins including analogs of such. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the desirable compositions, may be innumerable, and the enabled embodiments amount to only two. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe using any other HuR proteins other than those of amino acid sequence set forth in SEQ ID NO:3 or 4 and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims. It is suggested that by employing conventional claim language, the method claims be amended to include the specific soluble HuR proteins supported by the instant specification.

*In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Given the inherent unpredictability of physiological activity, which would include biological processes, a certain amount of enablement beyond mere assertion must be required.

The method of the instant claims comprises identifying an agent that has an inhibitory effect on complex formation between ARE-containing mRNA and an HuR protein, wherein said HuR protein is a soluble form of a recombinant full-length protein or variant or mutant thereof. A first consideration would be the breadth of the claims. The specification on page 5, lines 26-33, recites:

"We have found a soluble form of a HuR protein, i.e. a specific fragment comprising the physiological binding activity of the full-length HuR to ARE-mRNA of SEQ ID NO" 3 or SEQ ID NO:4; and, even more surprisingly, a full-length HuR protein of SEQ ID NO: 1 or SEQ ID NO:2, wherein the carboxylic acid of only one single amino acid, i.e. the C-terminal amino acid K, is esterified compared to the wild-type. Preferably said carboxylic acid of the C-terminal amino acid is esterified with an alkylmercapto-group, e.g. by use of 2-mercaptoethane-sulfonic acid or a salt thereof, e.g. sodium, to give the corresponding esterified HuR protein of SEQ ID NO: 1 or SEQ ID NO:2 in the form of a thioester.

Therefore, a method of using all soluble forms of HuR protein has not been enabled by the specification. The recitation of "soluble form" in claim 1, is not commensurate with the scope of the specification. Given the breadth of claim 1 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

***Claim Rejections - 35 U.S.C. § 112 second paragraph***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected as vague and indefinite because of several reasons.

Claim 1, line 1, is vague and indefinite because it recites "a method for identifying an agent that has an inhibitory effect" rather than the conventional 'a method for identifying an inhibitor".

Claim 1, line 2, is vague and indefinite because it recites "HuR" protein rather than "Hu-Antigen R". The metes and bounds of the term are unclear. It is suggested that the full name of the protein be recited at its first use in an independent claim.

Claim 1, line 6, is vague and indefinite because it recites "a candidate compound". Is this compound the agent? It is suggested that the name for the compound be recited in a consistent manner in the claims.

Claim 1, sub-part (d), is vague and indefinite because it fails to recite "and mixing (a) and (b) in the absence of (c)".

Claim 1, sub-part (f) recites the limitation "and/or non-complexed mRNA/protein species" in lines 10-11. There is insufficient antecedent basis for this limitation in the claim. Furthermore, the "or" limitation is unclear because the complexes should be compared with the non-complexed to obtain an amount.

Claim 1, sub-part (g) is vague and indefinite because it recites "choosing an agent which has an influence on the complex formation....". Is this agent the

inhibitor? Ii is suggested that the claim be amended to recite that the agent is one that inhibits complex formation between the ARE-containing mRNA and the HuR protein.

Claim 5, recites the limitation "the detection method" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claims 2-4, are rejected as vague and indefinite insofar as they depend on rejected claim 8 for their limitations.

***Conclusion***

No claim is allowed.

Claims 1-5 are rejected.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner

Art Unit 1646
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